REMARKS

Favorable consideration and allowance are respectfully requested for claims 1-2, 7-8 and 13-14.

The withdrawal of the previous claim rejections under 35 U.S.C. §§ 101, 102 and 112 are acknowledged with gratitude and the Examiner is thanked for the careful consideration of this application.

The rejection of claims 13 and 14 under 35 U.S.C. § 103(a) as obvious over Hikida et al. is respectfully traversed.

Claim 13 is directed to a method for determining the location of a sentinel lymph node and the presence of cancer metastasis by photodynamic therapy. The method involves the steps of administering an iminochlorine aspartic acid derivative of formula (I) or a pharmaceutically acceptable salt thereof and then detecting fluorescence with a fluorescent imaging system.

The recent Office Action correctly acknowledges that Hikida does not teach the use of the iminochlorine aspartic acid derivative of the compound of formula (I) of the present invention for determining the location of a sentinel lymph node and the presence of cancer metastasis by photodynamic therapy (PDT).

Despite this, the Examiner concludes that based on Hikida, one of ordinary skill in the art would expect that the administration of the compound (I) of the present invention would be successful in detecting the sentinel lymph node and as a result detecting the presence of metastasis.

Review of the reference reveals that none of the following words are ever mentioned: sentinel, lymph, node, and metastasis. Although the reference indicates that the compounds described therein might be useful for diagnosing cancer, based on the accumulability of the compound in cancer cells and the rapid excretion from normal cells, there is no indication anywhere in the reference that the compounds would accumulate in the sentinel lymph node. Further, there is no indication that aggregation of the compounds in the sentinel lymph node might be at all indicative of metastasis. The Office Action states that because the reference indicates the compounds would be useful as diagnostic agents, there would be an expectation that the compounds would be useful to detect the sentinel lymph node. However, there is no explanation, on the present record, of why these diagnostic agents of the reference would be useful to detect the sentinel lymph node.

Absent some teaching that these compounds would be useful to determine the location of a sentinel lymph node and to determine the presence of cancer metastasis, the cited reference fails to describe the required steps of the claimed method and cannot, therefore, render the claimed methods obvious. Indeed, the Office Action is entirely conclusory in asserting that the claimed invention is obvious and, as explained above, offers no complete reasoned explanation as to what would lead the skilled artisan from the teachings of the reference to the invention of claims 13 and 14.

As pointed out by the Supreme Court in KSR International Co. v. Teleflex Inc., 127 SCt 1727, 82 USPQ2d 1385, 1396 (U.S. 2007):

> [R]ejections on obviousness grounds cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness". (Quoting *In re Kahn*, 441 F.3d 977, 988, 78 USPQ2d 1329 (Fed. Cir. 2006) with approval).

Thus, to properly reject for obviousness, it is nevertheless necessary for the Examiner to articulate a convincing rationale as to what would lead a person skilled in the art to depart from the teachings of the prior art and strike out in the new direction claimed by applicants as their invention. Because the recent Office Action does nothing more than simply restate the invention of claims 13 and 14 and then conclude that this method would have been obvious, it follows that a proper, *prima facie* case of obviousness has not been made out, and the rejection should be withdrawn.

Accordingly, reconsideration and withdrawal of this rejection are respectfully requested.

The rejection of claims 1-2 and 7-8 under 35 U.S.C. § 103(a) over Hikida et al. in view of Levy.

Claims 1 and 2 are directed to a method for treating rheumatoid arthritis by photodynamic therapy. The method involves administering an iminochlorine aspartic acid derivative according to formula (I) or a pharmaceutically acceptable salt thereof.

Similarly, claims 7 and 8 are directed to a method for treating inflammatory keratosis by photodynamic therapy. The method involves administering an iminochlorine aspartic acid derivative according to formula (I) or a pharmaceutically acceptable salt thereof.

Again, the recent Office Action acknowledges that Hikida does not explicitly teach the use of an iminochlorine aspartic acid derivative according to compound (I) of the present invention for treating of rheumatoid arthritis or inflammatory keratosis.

The Office offers Levy as teaching that photodynamic therapy may have efficacy for psoriasis and autoimmune conditions, among other disorders. The Office Action equate psoriasis with inflammatory keratosis, however, psoriasis is but one of a number of conditions falling within the classification "inflammatory keratosis". In addition to psoriasis, "inflammatory keratosis" includes various forms of dermatitis and eczema, the broad class of papulosquamous disorders (of which psoriasis is but one among many), as well as the urticaria and erythema disorders. There is nothing in Levy which even suggests that the photodynamic therapy would be effective for treating all of the numerous and varied conditions falling within the classification "inflammatory keratosis". Accordingly, the skilled artisan would have no reason to modify the teachings of Levy so as to encompass treating inflammatory keratosis rather than psoriasis.

Further, Levy only discloses the potential indications for PDT, and there is no description of the actual treatments for these diseases using photosensitizers such as the compound of formula I of the present invention. Levy only teaches the possibilities of PDT therapy for these diseases, and moreover, the compound of formula I of the present invention is not suggested or described in Levy.

The skilled artisan would not be inclined to modify the teachings of Hikida based on the speculative assertions in Levy. Given that Levy provides no test

results or clinical data showing the efficacy of the compounds described therein to treat the presently claimed conditions, the skilled artisan would not simply accept that the treatment methods suggested by Levy would actually work. Further, the reference teaches that some photosensitizers have undesireable properties, for instance an activation wavelength of light that is too low, thereby preventing adequate light penetration and limiting the size and depth of tumors that can be treated. Other issues associated with known photosensitizers include the clearance rate of the compound, a rate that is too slow may preclude a patient from sunlight exposure. A clearance rate that is too fast may preclude adequate accumulation of the photosensitizer. Further, the rate and degree to which the compound selectively accumulates in tumors is important and certain minimum thresholds must be met before a compound can be suitable for photodynamic therapy.

Thus, the Levy reference suggests that not all photosensitizers are suitable for all photodynamic therapies. Still further, the broader implications of Levy's teaching that photosensitizer molecules will accumulate selectively in abnormal or hyperproliferative cells, that is, rapidly dividing or activated cells and neovasculature, suggests to the skilled artisan that the photosensitizer might accumulate in a wide variety of cells, thereby rendering photodynamic therapy unhelpful, or even dangerous, as in the case where the photosensitizer accumulates in cells where its effects are undesirable. Indeed, increasing photosensitivity in an organism is generally considered an adverse effect for many pharmaceutical compounds.

As such, not only would the skilled artisan not consider Levy to adequately teach a method of treating rheumatoid arthritis or inflammatory keratosis with photodynamic therapy, because the statements in Levy are speculative, the skilled artisan would not be inclined to try to substitute the photosensitizers described in the reference with other potential sensitizers.

Accordingly, the Office Action has not made out a proper showing of obviousness for the claimed methods of treatment in simply pointing to a reference which states that a claimed compound is a photosensitizer and then relying on a second reference which makes an unsubstantiated assertion that the claimed conditions are "potential indications for PDT", *see* Table 1 on page 16 of Levy.

The pending claims are directed to new methods of treatment. At best, the art suggests that other, significantly different, compounds *might* be suitable to treat the claimed conditions. However, the gap between the conjecture set forth in Levy and the kind of teaching that leads to a reasonable expectation of success is too great to allow the assertion of obviousness based on Levy to stand. Accordingly, reconsideration and withdrawal of this rejection are respectfully requested.

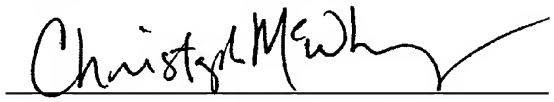
If there are any questions regarding this response or the application in general, a telephone call to the undersigned would be appreciated since this should expedite the prosecution of the application for all concerned.

If necessary to effect a timely response, this paper should be considered as a petition for an Extension of Time sufficient to effect a timely response, and

please charge any deficiency in fees or credit any overpayments to Deposit Account No. 05-1323 (Docket No. 101512.55677US).

Respectfully submitted,

November 13, 2008



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